Bevacizumab (Avastin®) for the Treatment of Age-Related Wet Macular Degeneration

Medical Policy

Section: Prescription Drug

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Description

Background: Age-related macular degeneration (AMD), characterized as a progressive degenerative disease of the macula, causes blindness in approximately 15 million people in the United States.

There are two forms of AMD: neovascular and non-neovascular. The non-neovascular form of AMD is more common and leads to a slow deterioration of the macula with a gradual loss of vision over a period of years. The neovascular (wet) form of the disease is responsible for the majority of cases of severe vision loss and is due to proliferation of abnormal blood vessels behind the retina. These blood vessels leak blood and fluid into the retina, resulting in visual abnormalities. The development of these abnormal blood vessels is due in part to the activity of vascular endothelial growth factor (VEGF), which induces angiogenesis, and increases vascular permeability and inflammation, all of which are thought to contribute to the progression of the neovascular (wet) form of AMD.

Ranibizumab (Lucentis®) has been approved by the FDA for the treatment of wet AMD by intraocular injection, while bevacizumab (Avastin®) has not, although it has been in common use as having a similar mechanism of action (Fung, et al.). The International Intra-vitreal Bevacizumab Survey was initiated to gather timely information regarding adverse events from physicians around the world using an internet based survey. A total of 70 centers from 12 countries reported on 7,113 injections performed on 5,228 patients. Physician-reported AE included corneal abrasion, lens Injury, endophthalmitis, retinal detachment, inflammation/uveitis, cataract progression, acute vision loss, central retinal artery occlusion, sub-retinal hemorrhage, retinal pigment epithelium tears, blood pressure elevation, transient ischemic attack, cerebrovascular accident and death. None of the AE rates exceeded 0.21%. The authors concluded that intra-vitreal bevacizumab is being used globally for ocular diseases. Self-reporting of AE following intra-vitreal bevacizumab injections did not reveal an increased rate of potential drug-related ocular or systemic events. These short-term results suggest that intra-vitreal bevacizumab appears safe.
Spaide, et al. (2006) described the short-term anatomical and visual acuity responses after intra-vitreal injection of bevacizumab in patients with CNV secondary to AMD. These investigators performed a retrospective study of patients with CNV secondary to AMD who were treated with intra-vitreal injection of bevacizumab (1.25 mg) during a 3-month period. The mean age of the patients was 80.3 years, the mean baseline visual acuity was 20/184, and 175 (69.7%) has inadequate response to alternate methods of treatment. At the 1-month follow-up (data available for 244 patients), the mean visual acuity was 20/137 (p<0.001 as compared with baseline), and 74 (30.3%) of patients had improvement in visual acuity as defined by a halving of the visual angle. At the 2-month follow-up (data available for 222 patients), the mean visual acuity was 20/122 (p<0.001), and 78 (31.1%) of patients had visual improvement. At the 3-month follow-up (data available for 141 patients), the mean visual acuity was 20/109 (p<0.001), and 54 (38.3%) of patients had visual acuity improvement. Patients underwent best-corrected Snellen visual acuity testing, optical coherence tomography, and ophthalmoscopic examination at baseline and follow-up visits. There were 266 consecutive eyes of 266 patients who received injections, and follow-up information was available for 251 (94.4%). The mean central macular thickness at baseline was 340 microns and decreased to a mean of 247 microns at month 1 (p<0.001) and 213 microns at month 3 (p<0.001). At 1 month, two patients had mild vitritis, as did one patient at 2 months, who had a history of recurrent uveitis. No endophthalmitis, increased intraocular pressure, retinal tear, or retinal detachment occurred. The risk for thromboembolic disorders did not seem to be different than reported previously in studies concerning macular degeneration. There were no apparent short-term safety concerns for intra-vitreal bevacizumab injection for CNV. Treated eyes had a significant decrease in macular thickness and improvement in visual acuity. The results of this study are in agreement with those of Inturralde et al (2006, 16 eyes/15 patients), Bashshur, et al. (2006, 17 eyes/17 patients), Rich, et al. (2006, 53 eyes/50 patients), and Avery et al (2006, 81 eyes/79 patients).

A German review on new treatments for neovascular AMD (authors not listed, 2006) stated that bevacizumab was among available therapeutic options. It concluded since bevacizumab (Avastin®) and ranibizumab are comparable in their pharmacological profile, bevacizumab may be an alternative in the off-label treatment of neovascular AMD. The switch to alternative treatment modalities should be considered in particular when the first line treatment is ineffective. The recommendations from this review provided evidence-based guidance for nonsurgical therapies in the management of neovascular AMD.

In an editorial on the use of intra-vitreal Avastin® as the low cost alternative to Lucentis® published in the American Journal of Ophthalmology, Rosenfeld (2006) state that "[c]urrently, there appears to be a global consensus that the treatment strategy using intravitreal Avastin® is logical, the potential risks to our patients are minimal, and the cost-effectiveness is so obvious that the treatment should not be withheld".

On March 20, 2006, a survey by the American Society of Retinal Specialists of its membership was completed. It found that 92% of 289 respondents felt intra-vitreal bevacizumab was "somewhat better" or "much better" than other FDA-approved or covered therapies. Only 4% of respondents had seen any thromboembolic complications thought to be related to the intra-vitreal bevacizumab, and 96% thought intra-vitreal bevacizumab was the same or better in terms of overall safety compared to other FDA-approved or covered therapies.

References:


**Policy**

Bevacizumab (Avastin®) may be considered medically necessary by intraocular injection for patients with age related wet macular degeneration as a cost-effective alternative to other agents.

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